202869

UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO
07/202,869	06/06/88	HOROSZEWICZ J	188

PENNIE & EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

HUTZELL, P. EXAMINER

ART UNIT	PAPER NUMBER
188	7

DATE MAILED: 12/28/90

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 9/7/90 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-42 are pending in the application.
   Of the above, claims 25, 27 and 32-42 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-24, 26, 28-31 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

15. Applicant's election without traverse of Group I, specie I in Paper No. 5 is acknowledged.

16. The receipt of an amended abstract is acknowledged. The specification does not substantiate the allegations of the abstract that the claimed monoclonal antibody has diagnostic and therapeutic utility because no evidence is presented which demonstrates that this is true.

17. The objection to claims 10, 11, and 28 under 37 CFR 1.75(c) is withdrawn in view of the amendment of the claims.

18. The rejection of claims 1-4, 7, 8, 11 and 14 under 35 USC §112, second paragraph is withdrawn in view of the amendment of the claims.

15 conc.

19. The specification is objected to and claim 15 is rejected under 35 USC § 112, first paragraph, as the specification fails to provide support for a claim drawn to a monoclonal antibody having the highly restricted binding specificity of that claimed in claim 12, wherein the antibody is a human antibody produced by a lymphocyte isolated from an individual with prostatic carcinoma. Given the high degree of unpredictability of successfully establishing stable cell lines producing human monoclonal antibodies, especially one having the particular claimed properties, and the lack of exemplary material demonstrating the feasibility of producing such a cell line, it is not clear that one of skill in the art could produce the claimed invention.

w/D

20. Claims 1-23 and 28-30 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the monoclonal antibody and cell line 7E11C and methods for its production and use, which are exemplified in the specification. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification discloses a single example of a cell line which produces a monoclonal antibody having the claimed properties. Given the limited exemplary material in support of the broad claims together with the unpredictability of producing further cell lines having the claimed properties, especially in view of the limited characterization of the antigen recognized by the 7E11C, it is not clear that one of skill in the art could produce further cell lines and antibodies having the claimed properties, based on the written specification alone. Accordingly, the claims should be limited to the antibody and cell line 7E11C disclosed in the specification.

21. The objection to the specification and rejection of claims 1-24, 26 and 28-31 under 35 USC §112, first paragraph are maintained. The declaration submitted with Paper No. 6 appears to be sufficient to overcome the rejection. However, a discrepancy is noted between the designations of the cell line identified in the ATCC Budapest Treaty Deposit conversion document and that disclosed in the specification. Applicant is requested to clarify the relationship between the 7E11C5 cell line identified in the ATCC document and the 7E11C cell line

described in the specification. Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and M.P.E.P. 608.01(p)(c) for further information concerning deposit practice.

22. The rejection of claim 1 under 35 USC § 112, first paragraph is withdrawn in view of the amendment of claim 1.

23. The rejection of claims 1-24, 26, and 28-31 under 35 USC § 102(a) over Horoszewicz et al. is withdrawn in view of the declaration filed under 37 CFR 1.131.

24. Claims 1-3, 10, 11, 20, and 28, 29 and 31 remain rejected under 35 USC 102(b)/103 over Frankel et al. for the reasons stated in the previous office action. Applicant's arguments have been carefully considered but are not found to be persuasive. Applicant states that the monoclonal antibodies taught by the reference are distinct from those claimed in their methods of production as well as in their tissue reactivities. For instance, Mabs 35 and 24 are said to be distinguished from applicant's antibodies in binding to kidney and salivary glands, respectively and in that both antibodies bind to breast carcinoma. However, the claims are not limited to antibodies which lack cross-reactivity to these tissues but are broadly drawn to monoclonal antibodies specific for a membrane-associated prostate epithelium-specific antigen, to a cell line produced using an immunogen derived from cells expressing organ or tissue-specific prostate antigens, and to methods for detecting prostate

antigens using the antibodies.

25. Claims 1-6, 10-14, 20-22 and 28, 29 and 31 remain rejected and claim 23 is rejected under 35 USC 102(b)/103 over Finstad et al. for the reasons set forth in the previous office action. Applicants arguments have been carefully considered but are not found to be persuasive. Finstad et al. teach IgG1 monoclonal antibody S27 which binds to an antigen present on normal and malignant human prostate epithelial membrane. Table 3 teaches that MAb S27 distinguishes between prostate carcinoma and other carcinomas, such as breast and colon carcinomas. Table 2 shows that the referenced antibody is unreactive with many normal human tissues tested. The reference is silent with respect to certain limitations of the claimed antibodies such as whether the S27 antigen is secreted, heterogeneity of staining of cells by S27, reactivity of S27 with bladder, urethra, or LNCaP cells, etc. However, the referenced antibody is presumed to be the same as those claimed in the absence of evidence to the contrary. The process limitations set forth in claims 10-14 are not construed as further limiting the claimed product as equivalent products are presumed to be obtainable by multiple routes absent evidence to the contrary. Applicant states on page 16 of the response that MAb S27 is distinct from those of applicant in being cross-reactive with various normal and malignant tissues. However, the claims are not limited to antibodies which lack cross-reactivity to these tissues. The burden is upon the applicants to

establish a patentable distinction between the claimed and referenced antibodies.

26. The rejection of claims 20-23 under 35 USC §102/103 over Webb et al. is withdrawn upon further consideration. The reference was improperly applied to claims 20-23 which are drawn to continuous cell lines producing antibodies which lack cross-reactivity to testis, because the cell lines taught by Webb et al. produce antibodies which bind to human testicle. Claims 1-3, 5, 7-11 28, 29, and 31 remain rejected under 35 USC 102(b)/103 over Webb et al. Webb et al. teach monoclonal antibody α-Pro-13 which is an IgG antibody specific for a membrane-associated non-secreted antigen present in prostate ductal epithelium, and which immunohistologically stains normal and prostatic cancer tissues. Applicant states that the referenced antibody is distinct from the claimed antibodies in cross-reacting with blood vessel endothelium, liver, trachea, tonsil, etc. and in lacking reactivity with LNCaP cells. However, the claims are not limited to antibodies which lack cross-reactivity with the tissues specified above or which bind to LNCaP cells. The burden is upon the applicants to distinguish between the claimed and referenced antibodies.

The rejection of claims 16, 17, and 19 under 102(b) is withdrawn in view of the teaching by Webb et al. that monoclonal antibody alpha Pro-13 binds to human testicle. The rejection of claims 16, 17, and 19 under 35 USC §103 over Webb et al. is

maintained. The claims are drawn to processes for producing monoclonal antibodies. Webb et al. teach the use of LNCaP cells as an immunogen in conventional methods of hybridoma production. Even if the claimed antibodies and hybridomas are distinguished over the prior art of record, the claimed processes for producing monoclonal antibodies are conventional and obvious over the prior art in the absence of evidence establishing the unobviousness of applying the conventional methods for the production of the claimed antibodies and hybridomas.

Rejections under 102/103 are applied in situations where applicant claims a composition in terms of function, property or characteristic where said function, property or characteristic is not explicitly shown by the reference. Each of the references applied in paragraphs 24-26 disclose products which appear to be identical to the claimed inventions, however the references are silent with respect to certain of the characteristics recited in the claims. These characteristics are considered to be inherent in the prior art in view of the numerous other similarities shared between the claims and the prior art, and in the absence of evidence to the contrary. These situations are not susceptible to Graham analysis because it is not apparent as to what, if any differences exist between the claims and the prior art. It is applicant's burden to identify any difference and to establish unobvious differences between the claimed products and the prior art.

27. Claims 1-3, 5-11, 16-20, 22, and 28-31 remain rejected under 35 USC §103 as obvious over Campbell in view of Frankel et al. or Webb et al. or Wright et al. Claims 1-3, 5 and 6 are drawn to monoclonal antibodies specific for membrane-associated prostate-associated antigen of normal and malignant human prostate epithelium and to said monoclonal antibodies which are of the IgG class and IgG1 subclass. Claims 7-11 are drawn to monoclonal antibodies having the previously described binding specificities which are produced by particular methods, claims 16-19 are drawn to processes for producing monoclonal antibodies, claim 20 is drawn to a cell line derived from a mouse immunized with cells bearing a prostate-specific antigen or determinant thereof derived from cells or tissues expressing prostate-specific antigens, claim 22 is drawn to a cell line obtained by immunizing a mouse with cells bearing a prostate-specific antigen or a determinant derived from LNCaP cells, and claims 28-31 are drawn to methods using monoclonal antibodies having the properties of those claimed in claims 1 or 2 to detect prostate cancer in human tissue or fluid samples. Campbell teaches the conventionality of methods for producing hybridomas and monoclonal antibodies as well as the utility of monoclonal antibodies for many different applications, including diagnostic assays. Frankel et al. teach monoclonal antibodies 35 and 24 which define membrane-associated antigens on normal and malignant prostate tissues. Webb et al. teach monoclonal antibody α-Pro 13, produced using a mixture of

cultured cells including LNCaP as the immunogen, which is specific for a membrane-associated, non-secretory, antigen present on normal and malignant prostate tissues and on prostate ductal epithelium. It would have been prima facie obvious to one of ordinary skill in the art to combine the teachings of the references and to substitute prostate-associated antigens such as prostate carcinoma tissues or cultured cell lines or extracts thereof, as immunogens into the conventional methods taught by Kipps et al. in order to produce antibodies specific for membrane-associated antigens found on normal and malignant prostate. It would have been obvious to use the claimed antibodies for the detection of prostate carcinoma-associated antigens in tissue or fluid samples in view of the teaching by Frankel et al., Wright et al., and Webb et al. that monoclonal antibodies specific for prostate were potentially useful for diagnosis of prostate carcinoma and for identification of metastases. One would have had a reasonable expectation of success in obtaining the claimed cell lines and antibodies in view of the teaching of Frankel et al. and Webb et al. that hybridomas and monoclonal antibodies having the broadly claimed properties were known. It would be expected that IgG and more specifically, IgG1 antibodies would be produced since antibodies of the IgG class and IgG1 subclass are isolated with high frequency using conventional hybridoma production methods. It would also have been expected that heterogeneous staining of

tissues would be observed using the antibodies since heterogenous antigen expression is frequently observed in tumors.

Even if the claimed antibodies and cell lines are distinguished over the prior art the processes for producing the monoclonal antibodies and methods of use recited in claims 16-19 and 28-31 are conventional and obvious over the prior art absent a showing of the unobviousness of applying these conventional methods to the claimed hybridomas and monoclonal antibodies.

The rejection of claims 4, 12-15, 21 and 23, 24, and 26 under 35 USC §103 is withdrawn upon further consideration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paula Hutzell whose telephone number is (703) 308-3533.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1096.

PH

Esther Kepplinger

ESTHER L. KEPPLINGER
SUPERVISORY PATENT EXAMINER
GROUP ART UNIT 182